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09/676,526	10/02/2000	Changsheng Liu	9046-034	5208

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51 Louisiana Avenue, N.W  
WASHINGTON, DC 20001-2113

EXAMINER
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MUTSCHLER, BRIAN L

ART UNIT	PAPER NUMBER
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1753

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/676,526

Applicant(s)

LIU ET AL.

Examiner

Brian L. Mutschler

Art Unit

1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-5, 10, 11 and 13-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-5, 10, 11 and 13-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 September 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 and 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
  - I. Claims 1, 6, 7 and 9, drawn to an electrophoresis separation system, classified in class 204, subclass 461.
  - II. Claims 2-5, 10, 11 and 13-16, drawn to a method of calibrating an electrophoresis system, classified in class 702, subclass 85.
  - III. Claim 8, drawn to a method of identifying nucleotides, classified in class 436, subclass 94.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions of Group I and Groups II and III are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus of group I can be used to perform different processes, such as analysis using imaging alone or for performing separations of molecules including proteins.
3. Inventions of Group II and Group III are distinct because the identification of nucleotides does not require the calibration of the electrophoretic apparatus.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Mr. Julius Fister on July 22, 2003 a provisional election was made without traverse to prosecute the invention of Group II, claims 2-5, 10, 11 and 13-16. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1 and 6-9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Specification***

7. The disclosure is objected to because of the following informalities:
- a. On page 2 at line 16, please change "having" to --have--.
  - b. On page 5 at line 20, please change "13a-13b" to --13a-13d--.
  - c. On page 5 at line 25, please change "Fig. 17" to --Figs. 17a-17g--.
  - d. The paragraph beginning at line 8 on page 8 is unclear.

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- e. On page 8 at line 22, please change "pick-picking" to --peak-picking--.
- f. On page 9 at line 12, please change "practical" to --practically--.
- g. On page 16 at line 28, please change "(G A, T or C)" to --(G, A, T or C)--.

Appropriate correction is required.

- 8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: METHOD FOR IN-SITU CALIBRATION OF ELECTROPHORETIC ANALYSIS SYSTEMS.

### ***Claim Objections***

- 9. Claims 13 and 14 are objected to because of the following informalities:
  - a. In claim 13 at line 6, please change "the said time-wavelength distribution" to either --the time-wavelength distribution-- or --said time-wavelength distribution--.
  - b. In claim 13 at line 12, please change "comprising of the *j* calibration vectors" to either -- comprising the *j* calibration vectors-- or -- comprised of the *j* calibration vectors--.
  - c. In claim 14 at line 1, please change "the method of isolating" to --the step of isolating--.

Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 2-5, 10, 11, and 13-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Simpson et al. (U.S. Pat. No. 6,017,434).

Regarding claim 2, Simpson et al. disclose a method of calibrating a detection system in an electrophoresis apparatus comprising a plurality of separation lanes and a detection system over a plurality of wavelength channels (spectral intensity bins) (col. 22, lines 1-30). At least one spectrum of light intensities is detected for each of a plurality of samples (col. 22, lines 1-30). Detected spectra are clustered into categories, and a calibration matrix (signature matrix) is created from the clusters (col. 22, line 1 to col. col. 23, line 12).

Regarding claim 3, spectra of at least some samples are discarded prior to clustering (col. 22, lines 1-49).

Regarding claim 4, a calibration matrix is determined for each of a plurality of separation lanes (col. 23, line 43 to col. 24, line 12).

Regarding claim 5, Simpson et al. disclose the use of up to 256 lanes, and a calibration matrix is created for each lane (col. 22, lines 1-29; col. 23, line 43 to col. 24, line 12).

Regarding claims 10 and 11, Simpson et al. disclose a method of automatically calibrating an electrophoretic separation apparatus having a plurality of separation lanes. A plurality of sets of light intensities is detected in a plurality of channels (col. 22, lines 1-29). Peaks are isolated in at least some of the plurality of sets of light intensities, and the number of dyes is estimated based on the isolated peaks (col. 23, line 43 to col. 24, line 12). Each peak is represented by a morphological formation (figs. 18A-18C). Coefficients are calculated for each separation lane based on the distribution of light and are arranged in a 4x4 matrix representing the number of dyes and channels (spectral bins) (col. 23, line 43 to col. 24, line 12).

Regarding claim 13, the method of Simpson et al. samples light emitted from species having a chromophore over a number of wavelength channels and a number of time intervals to form a time-wavelength distribution (figs. 18A-18C; col. 22, lines 1-29). peaks are isolated and clustered into classes, which are used to form a calibration matrix (signature matrix) of calibration vectors (col. 22, line 1 to col. 24, line 12).

Regarding claim 14, within each channel (spectral bin), noise is removed by filtering and the three highest peaks were isolated from the series of peaks according to width and spacing (col. 23, line 43 to col. 24, line 12).

Regarding claim 15, filters are used to identify the peaks (col. 23, lines 25-42).

Regarding claim 16, peaks are isolated by scanning and comparing the shapes of the peaks (col. 23, line 43 to col. 24, line 12).

Since Simpson et al. teach all of the limitations recited in the instant claims, the reference is deemed to be anticipatory.

12. Claims 2, 3, 10, 11, and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Labrenz (U.S. Pat. No. 6,333,501).

Regarding claim 2, Labrenz discloses a method of calibrating a detection system in an electrophoresis apparatus comprising at least one separation lane and a detection system configured to sense a spectrum of light intensities over a number of wavelength channels (col. 6, lines 41-56). At least one spectrum is detected for each of a plurality of samples (col. 1, lines 41-56). The spectra are clustered into a number of categories based on similarities, and a calibration matrix is created from the clusters (col. 8, line 32 to col. 12, line 19).

Regarding claim 3, at least some sample spectra are discarded prior to clustering (col. 7, lines 48-56).

Regarding claims 10 and 11, Labrenz discloses detecting a plurality of sets of light intensities in a number of channels (col. 6, lines 41-56). Peaks from at least some of the plurality of sets of light intensities are isolated and the number of dyes is estimated based on the isolated peaks (col. 8, line 32 to col. 9, line 35). Coefficients are calculated and arranged to form a matrix based on the number of channels and the number of dyes (col. 9, line 9 to col. 12, line 19).



Regarding claim 13, Labrenz discloses sampling light from species having a chromophore over a number of wavelength channels (spectral bins) and a number of time intervals (col. 6, lines 41-56). Discrete species are represented by morphological formations (col. 6, line 57 to col. 8, line 43). Peaks are isolated from the formations and clustered based on similarities (col. 7, line 48 to col. 8, line 43). A calibration matrix is formed based on calibration vectors that represent the clusters (col. 9, line 9 to col. 12, line 9).

Regarding claim 14, the data is preprocessed and a number of peaks are isolated (col. 8, lines 5-43). Peaks are further selected from the isolated peaks according to width and spacing (col. 8, lines 32-43).

Regarding claim 15, morphological filters are used to isolate peaks (col. 8, lines 32-43).

Since Labrenz teaches all of the limitations recited in the instant claims, the reference is deemed to be anticipatory.

### ***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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14. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Labrenz (U.S. Pat. No. 6,333,501), as applied above to claims 2, 3, 10, 11, and 13-15, and further in view of Simpson et al. (U.S. Pat. No. 6,017,434).

Labrenz discloses a method having all of the limitations recited in claims 2, 3, 10, 11, and 13-15 of the instant invention, as explained above in section 12.

The method of Labrenz differs from the instant invention because Labrenz does not disclose the that a calibration matrix is determined for each of a plurality of separation lanes, as recited in claim 4, and that at least 96 calibration matrices are generated, as recited in claim 5.

Simpson et al. teach a similar method of calibrating a detection system in an electrophoretic apparatus comprising a plurality of separation lanes. The detection system is capable of simultaneously detecting up to 256 lanes (col. 22, lines 1-29). A calibration matrix is created for the four spectral bins of each lane (col. 23, line 43 to col. 24, line 12).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the method of Labrenz to use a plurality of separation lanes and creating a calibration matrix for each lane as taught by Simpson et al. because using a plurality of separation lanes each with its own calibration matrix allows for the simultaneous separation of a plurality of samples.

**Conclusion**


15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US 6,015,667	Sharaf
US 2002/0125136 A1	Sharaf et al.
US 2002/0166767 A1	McVey et al.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian L. Mutschler whose telephone number is (571) 272-1341. The examiner can normally be reached on Monday-Friday from 7:30am to 4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1300.

  
NAM NGUYEN  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1700

blm  
January 22, 2004